



Holmes, E. A., O'Connor, R. C., Perry, V. H., Tracey, I., Wessely, S., Arseneault, L., Ballard, C., Christensen, H., Cohen Silver, R., Everall, I., Ford, T., John, A., Kabir, T., King, K., Madan, I., Michie, S. F., Przybylski, A. K., Shafran, R., Sweeney, A., ... Bullmore, E. (2020). Multidisciplinary research priorities for the COVID-19 pandemic: a call for action for mental health science. *Lancet Psychiatry*, 7(6), 547-560. [https://doi.org/10.1016/S2215-0366\(20\)30168-1](https://doi.org/10.1016/S2215-0366(20)30168-1)

Peer reviewed version

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[10.1016/S2215-0366\(20\)30168-1](https://doi.org/10.1016/S2215-0366(20)30168-1)

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## **Multidisciplinary research priorities for the COVID-19 pandemic: a call for action for mental health science**

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## **Multidisciplinary research priorities for the COVID-19 pandemic: a call for action for mental health science**

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### **Abstract**

The COVID-19 pandemic is having a profound effect on all aspects of society, including mental health as well as physical health. We explore the psychological, social and neuroscience impacts of COVID-19, and set out immediate priorities and longer-term strategies for mental health science research. These priorities were informed by surveys of the public and an expert panel convened by the UK Academy of Medical Sciences and the mental health research charity, MQ: Transforming Mental Health, in the first weeks of the pandemic in the UK in March 2020. We urge UK research funding agencies to work with researchers, people with lived experience and others to establish a high level co-ordination group to ensure that these research priorities are addressed, and to allow new ones to be identified over time. The need to maintain high quality research standards is imperative. International collaboration and a global perspective will be beneficial. An immediate priority is collecting data on the mental health impacts of the COVID-19 pandemic across the whole population and vulnerable groups, and on brain function, cognition and mental health for COVID-19 patients. There is an urgent need for research to address how mental health consequences for vulnerable groups can be mitigated under pandemic conditions, as well as on the impact of repeated media consumption and health messaging around COVID-19. Discovery, evaluation and refinement of mechanistically-driven interventions to address the psychological, social and neuroscientific aspects of this pandemic are required. Rising to this challenge will require integration across disciplines and sectors, and should be done together with people with lived experience. New funding will be required to meet these priorities, but it can be efficiently leveraged by the UK's world-leading infrastructure.

### **1. Introduction**

It is already evident that the direct and indirect psychological and social impacts of the pandemic are pervasive, and could affect mental health now and into the future. The pandemic is occurring against the backdrop of increased prevalence of mental health issues in the UK in recent years in some groups<sup>1,2</sup>. Furthermore, SARS-CoV2, the virus causing COVID-19, might infect the brain or trigger immune responses that have additional adverse effects on brain function and mental health in COVID-19 patients.

Research funders and researchers must deploy resources to understand the psychological, social and biological impacts of the COVID-19 pandemic. Mobilisation now will allow us to apply the learnings gained to any future periods of increased infection

and lockdown, which will be particularly important for frontline workers, and for vulnerable groups. We propose a framework for the prioritization and coordination of essential, policy-relevant psychological, social and neuroscience research, to ensure that any investment is efficiently targeted on the critical mental health science questions as the pandemic unfolds. We use the term 'mental health sciences' to reflect the many different disciplines, including but not limited to psychology, psychiatry, clinical medicine, behavioural and social sciences and neuroscience, that will need to work together in a multidisciplinary fashion together with people with lived experience to address these research priorities.

The UK has powerful advantages in mounting a successful response to the pandemic, including strong existing research infrastructure and expertise, but the community must act rapidly and collaboratively if it is to deal with the growing threats to mental health. A fragmented research response, characterized by small-scale and localized initiatives, will not yield the clear insights necessary to guide policy-makers or the public. Rigorous scientific and ethical review of protocols and results remains the cornerstone of safeguarding participants and upholding research standards. Deploying a mental health science perspective<sup>3</sup> to the pandemic will also inform population-level behaviour change initiatives aimed at reducing the spread of the virus. International comparisons will be especially helpful in this regard. In this paper, we explore the psychological, social and neuroscience impacts of COVID-19, and set out clear, immediate priorities and longer-term strategies for each of these aspects.

We also conducted surveys of the public and people with lived experience of mental ill-health. The general population survey, conducted by Ipsos MORI, revealed widespread concerns about the impact of social isolation or social distancing on wellbeing; increased levels of anxiety, depression, stress and other negative feelings; and concern about the practical implications of pandemic response including financial difficulties. The prospect of becoming physically unwell with COVID-19 ranked lower than these issues related to the social response to the pandemic. The MQ stakeholder survey of people with lived experience of a mental health issue likewise highlighted general concerns about social isolation and increased levels of anxiety and depression. More specifically, stakeholders frequently expressed concerns about exacerbation of pre-existing mental health issues, greater difficulty in accessing mental health support and services under pandemic conditions, and impact of COVID-19 on the mental health of family members, especially children and older people. Both surveys are reported in full in the web appendix. These findings, combined with the published scientific literature, informed the development of our research priorities. They represent a snapshot of the current situation, but will need to be repeated more rigorously over the course of the pandemic.

#### **Panel 1: Methodology**

This article summarises the priorities put forward by an interdisciplinary group of 24 world-leading experts, including people with lived experience, from across the bio-psycho-social spectrum of expertise in mental health science in March/April 2020. The experts were convened by the UK Academy of Medical Sciences and the mental health research charity, MQ: Transforming Mental Health. Members participated in an individual capacity, not as representatives of their organisations. A coordinating group of seven experts met daily over a period of two weeks to develop the research priorities, informed

by input from the expert advisory group. Given the need to develop the research priorities rapidly to inform immediate funding priorities, extended evidence gathering and consultation was not possible. However, we are confident that the wide breadth of expertise on the expert group and their leading roles in their respective fields provide a wide-ranging and comprehensive view of the mental health and neuroscience research priorities.

Lived experience was incorporated by four mechanisms. First, three lived experience representatives provided input via the expert advisory group. Second, an online survey collected data on people's two biggest concerns about the mental health and wellbeing implications of the COVID-19 pandemic, as well as coping strategies. The survey was promoted via email to MQ's supporter network as well as via social media. In total, 2,198 people completed the survey, submitting 4,350 concerns about the mental health impacts of the COVID-19 pandemic and 1,987 responses about what has helped maintain mental health and wellbeing during the pandemic. A thematic analysis of the full dataset was carried out. Third, two questions were asked on Ipsos MORI's online Omnibus survey to collect data on people's concerns about the impact of COVID-19 on mental wellbeing, as well as what is helping people's mental wellbeing at this time. In total, 1,099 interviews were completed with adults aged between 16 and 75 across England, Wales and Scotland. Quotas were set and data were weighted to the offline population to ensure a nationally representative sample by gender, age and region. Statistical analysis was carried out and any sub-group differences included are statistically significant at a 95% confidence interval unless stated otherwise. A summary report of the findings of both surveys and further methodological details can be found in the web appendix. The Ipsos MORI tabular data can be found on its website<sup>4</sup>. Fourth, the manuscript was peer-reviewed by a reviewer with lived experience of a mental health issue. We acknowledge the limitations of our surveys, including the representativeness of the MQ sample, the short timescale for input and the representativeness of online populations. We also acknowledge the limited evidence gathering and opportunity for wider consultation of people with lived experience. However, combined, these four mechanisms of collecting input from people with lived experience provide important insight into people's concerns about the impact of COVID-19 on mental health and coping strategies within the very limited timeframe.

A living systematic map<sup>5</sup> is tracking emerging empirical studies, systematic reviews, and modelling on COVID-19. As of 1<sup>st</sup> April 2020, 643 were records identified in the databases MEDLINE and Embase. Only 10 of these were on mental health impacts of the pandemic<sup>6-15</sup>.

## **2. Psychology and individual factors: researching the impact of COVID-19 on mental health**

In this section, we focus on the psychological and individual processes in COVID-19, such as cognition, emotion and behaviour, which affect mental health. Two areas that require urgent research prioritisation are:

### **(1) What is the impact of COVID-19 on risk of anxiety, depression, self-harm, and suicide, and other mental health issues?**

While a rise in anxiety symptoms and coping responses to stress are expected during these extraordinary circumstances, there is a risk that prevalence of clinically-relevant levels of anxiety, depression and other harmful behaviours, such as suicide and self-harm, will increase. It is important to note, however, that a rise in suicide is not inevitable especially with national mitigation efforts<sup>16</sup>.

The potential fallout of an economic downturn on mental health is likely to be profound on those directly affected as well as on their caregivers. The SARS epidemic was associated with a 30% increase in suicide among those aged 65 and older; around 50% of recovered patients remained anxious; and 29% of health care workers experienced probable emotional distress<sup>17-19</sup>. Patients who survived severe and life-threatening illness were at risk of post-traumatic stress disorder and depression<sup>18,19</sup>. Many of the anticipated consequences of quarantine<sup>13</sup> and associated social/physical distancing measures are themselves key risk factors for mental health issues. These include suicide and self-harm, alcohol and substance abuse, gambling, domestic and child abuse, as well as psychosocial risks, such as social disconnection, lack of meaning or anomie, entrapment, cyberbullying, feeling a burden, financial stress, bereavement, loss, unemployment, homelessness and relationship breakdown<sup>20-22</sup>.

A major adverse consequence of the COVID-19 pandemic is likely to be increased social isolation and loneliness (as reflected in our surveys), which are strongly associated with anxiety, depression, self-harm and suicide attempts across the lifespan<sup>23,24</sup>. Tracking loneliness and intervening early are important priorities. Critically, reducing sustained feelings of loneliness is a candidate mechanism to protect against suicide, self-harm and emotional problems<sup>25,26</sup>. Social isolation and loneliness are distinct and may represent different risk pathways.

To inform management of the pandemic it is vital to understand the socioeconomic impact of the policies used to manage the pandemic, which will inevitably have serious effects on mental health by increasing unemployment, financial insecurity and poverty<sup>27,28</sup>. Involvement of people with lived experience and rapid qualitative research with diverse people and communities may help to identify ways in which this negative impact might be alleviated. Achieving the right balance between infection control and mitigation of these negative socioeconomic impacts must be considered<sup>29</sup>.

### ***Immediate research priorities***

**Monitor and report rates of anxiety, depression, self-harm, suicide, as well as other mental health issues both to understand mechanisms and critically to inform interventions.** This should be across the general population and vulnerable groups, including frontline workers. Monitoring must go beyond NHS record linkage to capture the real incidence in the community as self-harm may become more hidden. We must harness existing datasets and ongoing longitudinal studies, and also establish new cohorts with new ways of recording including detailed psychological factors<sup>25,30</sup>. Techniques assessing moment to moment changes in psychological risk factors should be embraced .

### ***Longer-term strategic research programmes***

Given the unique circumstances of COVID-19, data will be vital to determine causal mechanisms associated with poor mental health<sup>30,31</sup>, including loneliness and entrapment. To optimize effectiveness, psychological treatments need to be mechanistically-informed, that is both causally associated with poor mental health and modifiable by an intervention<sup>30</sup>. A 'one-size fits all' response will not suffice, as the effectiveness of interventions can vary across groups<sup>25,32–35</sup>. **Digital psychological interventions that are mechanistically informed, alongside better understanding of the buffering effects of social relationships during stressful events, are required in the long-term.** The digital response is crucial<sup>36–38</sup>, not only because of social isolation measures but also because less than a third of people who die by suicide have been in contact with mental health services in the 12 months before death<sup>39</sup>. Digital interventions for anxiety, depression, self-harm and suicide include: information provision; connectivity and triage; automated and blended therapeutic interventions, such as apps and online programmes; phone calls and messages to reach those with more limited digital resources (digital poverty)<sup>40</sup>; suicide risk assessments; chatlines and forums; and technologies that can be used to monitor risk either passively or actively. The digital landscape extends beyond apps and requires an evidence-base. Artificial intelligence driven adaptive trials could help evaluate effectiveness while digital phenotyping could be helpful to ascertain early warning signs for mental ill health<sup>41</sup>.

Looking beyond digital interventions, as not everyone has access to them (e.g. digital poverty), it is important to ascertain what other mechanistically-based psychological interventions are effective and for whom<sup>30,42</sup>. Risks and buffers for loneliness should be a focal target in interventions to protect wellbeing. The longer-term consequences of COVID-19 on the young and older generations (and other high risk groups including the frontline workforce, those with existing mental health conditions, and caregivers) are also unknown and must be a priority.

### **(2)How do individuals build optimal structures for a mentally healthy life that works for them in the wake of COVID-19 and social/physical distancing?**

The optimal structure of a mentally healthy life for individuals in the wake of COVID-19 needs to be mapped out. This will vary as a function of background and individual circumstances. Changes in sleep and lifestyle behaviours influence our mental health and stress response. Understanding the effective, individualized ways of coping in such a situation is of paramount importance<sup>43–45</sup>. The social and personal resources (e.g. seeing family and getting sufficient sleep) available to individuals can be important resilience-related factors for mitigating mental health difficulties under particularly stressful circumstances<sup>46</sup>. We need research to foster positive social resources, resilience and altruism.

### ***Immediate research priorities***

**Understanding how frontline health and social care staff and their families can be supported to optimize coping strategies could mitigate symptoms of stress, and facilitate the implementation of preventative interventions in future<sup>47,48</sup>.**

Under COVID-19 it is important that health and social care workers are supported to stay in work; the personal, social and economic benefits are vast. Personalized psychological approaches are likely to be a key component to address complex mental health conditions, coping and prevention<sup>30</sup>. Given the association between sleep disturbance and mental health<sup>49</sup>, research on mitigating the impact of such changes on our mental health and stress response is required. Indeed, there is an established relationship between the latter and suicide risk<sup>50</sup>.

### ***Longer-term strategic research programmes***

**Develop novel interventions to protect mental wellbeing, including those based on positive mechanistic-based components (i.e. causal, modifiable factors) such as altruism and prosocial behaviour.** This could include increased opportunities to elicit community support<sup>51,52</sup>; exercise<sup>53</sup>, social activities<sup>54</sup>, training in assertiveness and conflict resolution<sup>55</sup>; and group interventions that provide support through peers<sup>56</sup>.

The inclusion of altruism in UK Government health messages has likely impacted positively on wellbeing compared to compulsory orders to stay at home<sup>47</sup>. Key research questions include: What altruism-based psychological interventions can be developed for mental wellbeing derived from theories of altruism and prosocial behaviour? What can be learned from the large-scale roll-out of volunteer-based psychological interventions that will optimise the benefits to individuals and society?

Home working, loss of employment and social/physical distancing have abruptly interrupted many social opportunities important to physical and psychological health. It is important to research the mental health dimension of online life, and investigate how changes in engagement with gaming and online platforms might inform interventions aimed at improving mental health. **We must rapidly learn from successful existing strategies to maintain and build social resources and resilience, as well as promote good mental health, in specific populations moving forward.**

**Table 1. Psychology and individual factors: the impact of COVID-19 on mental health**

<b>Psychology and Individual factors</b>	<b>Immediate actions</b>	<b>Longer term strategic programmes</b>
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<p><b>What is the impact of COVID-19 on risk of anxiety, depression, and outcomes such as self-harm and suicide?</b></p>	<p>Improve monitoring and reporting of the rates of anxiety, depression, self-harm, suicide as well as other mental health issues</p> <p>Determine the efficacy of mechanistically-based digital and non-digital interventions and evaluate optimal model(s) of implementation</p>	<p>Determine the mechanisms (e.g. entrapment and loneliness) that explain the rates of anxiety, depression, self-harm and suicide</p> <p>Understand the role of psychological factors in buffering the effect of social context on mental health issues</p> <p>Ascertain the longer-term consequences on wellbeing of COVID-19 on the young and older generations (and vulnerable groups)</p>
<p><b>What is the optimal structure for a mentally healthy life in the wake of COVID-19 and social/physical distancing?</b></p>	<p>Determine what psychological support is available to support frontline medical and health care staff and their families</p> <p>Understand the psychological (e.g. coping), physiological (e.g. sleep, nutrition) and structural (e.g. rotas) factors that protect as well as adversely affect mental health</p>	<p>Develop novel interventions to protect mental wellbeing, including those based on positive mechanistic-based components such as altruism and prosocial behaviour and understanding of online life</p> <p>Understand how we optimize positive social resources and enhance resilience in the face of stress</p> <p>Establish the effects of altruism on mental health and wellbeing in the wake of COVID-19</p>

### 3. Social and population factors: the impact of COVID-19 on mental health

Population level factors, such as the impact of social distancing measures (more recently being re-described as physical distancing<sup>57</sup>) and other necessary public health measures, affect mental health within a syndemics approach (Table 2). By syndemics we mean

intersecting global trends among demographics (e.g. aging, rising inequality) and health conditions (e.g. chronic diseases, obesity) that yield resultant co-morbidities. These interacting health effects and societal forces that fuel them combine to form syndemics, or complex knots of health determinants<sup>58</sup>. Research priorities around COVID-19 require us to embrace complexity by deploying multidimensional perspectives. Three areas that require urgent research prioritisation are:

**(1) What are the mental health consequences of the COVID-19 lock down and social isolation for vulnerable groups, and how can these be mitigated under pandemic conditions?**

We do not yet know the immediate or long term consequences of the COVID-19 lock down and social isolation on mental health. While worries and uncertainties about a pandemic are common, for some they can cause undue distress as well as impairment to social and occupational functioning<sup>13,59,60</sup>. Across society, a sense of loss can stem from losing direct social contacts, and also range from loss of loved ones, to loss of employment, educational opportunities, recreation, freedoms and supports. Existing evidence suggests some measures taken to control the pandemic may have a disproportionate effect on those most vulnerable (Panel 2).

Vulnerable groups include those with pre-existing mental and/or physical health issues including those with SMI (Severe Mental Illnesses), recovered individuals, and those who become mentally unwell, for example in response to anxiety surrounding the pandemic<sup>47,61,62</sup> (Panel 2). Therefore, loss of access to mental health support, alongside loss of positive activities, will increase vulnerability during COVID-19 lockdown. Increased anxiety and depression in response to the outbreak has been widely reported<sup>63</sup>. Health workers who come in close contact with the virus and are exposed to traumatic events such as death and dying, and also making highly challenging decisions, are particularly at risk of stress responses<sup>9</sup>.

The pandemic intersects with rising mental health issues in childhood and adolescence<sup>2,64,65</sup>. Ascertaining and mitigating effects of school closures for youth seeking care is urgent and essential, given school is often a first port of call<sup>64,66</sup>, considering vulnerabilities such as special educational needs and developmental disorders, and finding therapeutic levers<sup>67</sup>. For the older population, promoting good mental health is important during self-isolation, which can be compounded by lifestyle restrictions, exacerbated loneliness, co-morbidities such as dementia, feelings of worry and guilt for utilizing resources<sup>68</sup>. There is an acute need to identify remotely-delivered interventions that support those at risk of abuse<sup>69,70</sup>.

***Immediate research priorities***

**To reduce mental health issues and boost resilience generally, and in vulnerable groups in particular, a co-ordinating mechanism for pandemic mental health interventions is required for (1) the agile identification of interventions that can be repurposed, alongside identification of gaps which will require bespoke de novo design, and (2) the evaluation and roll-out of bespoke remotely-delivered interventions.** By the term 'intervention', we mean interventions of all sorts that make a difference to mental health including population

level policy, occupational guidelines, psychological interventions (see earlier section) and so forth.

We need to rapidly gather high quality data to ascertain effects over time. Innovative research is needed to establish ways to mitigate and manage mental health risks and inform interventions under pandemic conditions.

Research to support vulnerable groups needs to consider cross-cutting themes, such as: in the physical absence of schools and clinics, creating methods to provide connectivity and support; rapid innovation in mental health services that can be remotely signposted and delivered, including online clinics and community support; identifying and evaluating means to support those at risk of abuse within the home, including online outreach; and swiftly providing interventions to promote mental well-being in frontline health workers. **By identifying cross-cutting research themes, interventions to help specific vulnerable populations should be leveraged to help other vulnerable groups.**

### ***Longer-term research priorities***

Health services research must reliably and iteratively inform remotely delivered mental health resources, such as digital clinics to efficiently manage mental health issues in an adaptive and flexible manner<sup>71</sup>. This requires a co-ordinating mechanism to prioritise and streamline efforts, working with service users to optimise signposting and delivery, as well as defining therapeutic targets that matter from a user perspective (e.g. loss, loneliness). It requires a range of disciplines including psychology, digital science and social sciences<sup>72</sup>. International collaboration will ensure the necessary research skills and expertise. Research should harness internet-based social media and gaming using existing platforms, and be cognisant of a digital divide that leaves 15% of Britons without internet access<sup>73</sup>.

Research for population-level interventions will require rapid evolution of approaches, starting with testing whether existing digital interventions can be repurposed, such as physical activity, sleep and stress management programmes, as well as targeted approaches for prevention and treatment of established mental health symptoms (e.g. anxiety and worry<sup>74</sup>). Tailoring of such universal interventions will need to be informed by experimental and social science, for example for loneliness befriending and physical activity<sup>75,76</sup>. The effectiveness of arts-based interventions also needs to be assessed<sup>77</sup> as other generative activities that boost positive coping and resilience throughout society, from community-based activities to enhance life-skills to exercise outdoors (see lived experience surveys). The effectiveness of all interventions requires rigorous evaluation and implementation to avoid issuing a “plethora of unknown apps”<sup>78</sup>. Interventions at the population level should be repurposed, developed and tested in a virtuous loop to create the necessary evidence base.

### **(2) What is the impact of repeated media consumption about COVID-19 in traditional and social media on mental health and how can wellbeing be promoted?**

People seek trusted information via the media, which can provide swift, critical guidance regarding the pandemic. Media consumption can be adaptive and positive for mental

health. However, reports of infectious diseases often use risk-elevating messages, which can amplify public anxiety<sup>79</sup>. Social media can be a source of rapidly disseminated misinformation<sup>80</sup>, amplifying perceptions of risk<sup>81</sup>. Repeated media exposure to information about an infectious disease particularly can exacerbate stress responses, amplify worry and impair functioning<sup>82</sup>. Anxiety and uncertainty can drive additional media consumption and further distress, creating a cycle that can be difficult to break<sup>83</sup>. Media-fuelled distress can promote behaviours that negatively impact the healthcare system (e.g. visits to emergency departments, hoarding of face masks), with downstream mental and physical health consequences<sup>84</sup>.

### ***Immediate research priorities***

**There is an urgent need to better understand the role of repeated media consumption around COVID-19 in amplifying distress and mental ill-health in various groups, as well as the optimal patterns of consumption to promote wellbeing.** Research is needed to inform future approaches including strategies to: help individuals to stay informed by authoritative sources; prevent over-exposure to media; and mitigate and help manage the impact of viewing images with traumatic content.

### ***Longer-term research priorities***

**Research should inform evidence-based guidelines for media around pandemic reporting**, for example clearly identifying authoritative sources, limiting graphic footage and encouraging social media companies to flag or correct disinformation and rumours. Research should help develop **strategies to mitigate individuals' risk of exposure to misinformation and amplification of anxiety**, for example by minimizing sharing of misinformation and strategies for managing the emotional consequences. Adaptive and positive uses of traditional and social media such as influencers should be understood and harnessed. Knowing the impact of pandemic media on various vulnerable groups, such as at risk children, is critical.

### **(3)What are the best methods for promoting successful adherence to behavioural advice about COVID-19 whilst enabling mental wellbeing and minimising distress?**

Behavioural change – such as the three personal protective behaviours of handwashing, not touching the T-zone and tissue use, and social/physical distancing required to control the pandemic – necessitates ensuring people know what to do, are motivated to do it and have the skills and opportunity to enact the changed behaviours<sup>85,86</sup>. Messaging is key for good knowledge<sup>86</sup>, but public health messaging needs to draw on behavioural science if it is to be effective and avoid unintended consequences. We know that the more concerned people are in pandemics, the more likely they are to adhere to advice<sup>87</sup>. Increasing concern, however, may heighten distress, which could undermine adherence or exacerbate existing mental health issues. Anxiety can be fuelled by uncertainty, and also by fears of risk of harm to self or others. For example, feelings of paranoia<sup>88</sup> can be heavily influenced by anxiety, while symptoms of OCD<sup>89</sup> can be associated with fear of contagion and rigid handwashing<sup>90</sup>. Increasing people's confidence and clarity in what they need to do fosters adherence to health behaviours<sup>91</sup>, and can help people to manage psychological distress.

### ***Immediate action***

**Research on COVID-19 health messaging is urgently required to both optimise health behaviour change, and reduce unintended mental health issues, which will be required in the event of a second wave of infection.** Research should prioritise message content, format and delivery modes and behavioural change alongside risk communication, and consider how this may need to vary for diverse groups. A virtuous cycle which tracks perceptions of and responses to public health messages during this pandemic will enable iterative improvements. It must be informed by mental health science<sup>3</sup> to close the gap, for example, between effective behaviour messages and maladaptive consequences.

### ***Longer-term research priorities***

**It will be vital to create an evidence base of lessons learned to plan for future pandemics.** That is, detailing how to foster a rapid and coordinated response regarding health messaging from governments<sup>92</sup> and simultaneously to develop effective systems embedded in communities to reach out and access the most vulnerable groups in our society, including: 1) how to motivate and enable people to prepare psychologically and plan practically for possible future scenarios; and 2) how to promote people's care and concern for others, fostering a sense of collective solidarity and altruism. The optimal messaging should be tailored (including digitally) to different social groups to connect diverse segments of the population to appropriate mental health information resources.

**Table 2. Social and population factors: the impact of COVID-19 on mental health**

<b>Social and group factors</b>	<b>Immediate action</b>	<b>Longer term programmes</b>
<b>What are the mental health consequences of the COVID-19 lock down and social isolation for vulnerable groups, and how can these be mitigated under pandemic conditions?</b>	<p>Determine best ways of signposting and delivering mental health services for vulnerable groups, including online clinics and community support. Identify and evaluate outreach means to support those at <i>risk of abuse</i> within the home.</p> <p>Ascertain which evidence-based interventions can be rapidly repurposed at scale for the current pandemic, and identify gaps requiring bespoke remotely-delivered interventions to boost resilience and reduce mental health issues.</p>	<p>Based on gaps identified, design bespoke approaches for population-level interventions targeted at (a) prevention and treatment of mental health symptoms (e.g. anxiety) and (b) boosting coping and resilience (e.g. exercise).</p> <p>Innovation for novel universal interventions on new mechanistically-based targets from experimental and social sciences (e.g. for loneliness befriending; gaming initiatives) that can help mental health.</p> <p>Assess the effectiveness of arts-based and life-skills based</p>

	Swiftly provide interventions to promote mental well-being in frontline health workers exposed to stress and trauma that can be delivered now and at scale.	interventions and other generative activities including exercise outdoors.
<b>What is the impact of repeated media consumption about COVID-19 in traditional and social media on mental health and how can wellbeing be promoted?</b>	<p>Understand the role of repeated media consumption in amplifying distress and anxiety, as well as optimal patterns of consumption for wellbeing.</p> <p>Develop strategies to prevent over-exposure to anxiety-provoking media; including how to encourage diverse populations to stay informed by authoritative sources they trust. Mitigate and manage the impact of viewing distressing footage.</p> <p>Mitigate and manage the impact of viewing distressing footage.</p>	<p>Inform evidence-based media policy around pandemic reporting (e.g. clearly identify authoritative sources, encourage companies to correct disinformation, traumatic footage).</p> <p>Mitigate individuals' risk of misinformation (e.g. improve health literacy and critical thinking skills, minimize sharing of misinformation).</p> <p>Understand and harness positive uses of traditional media, online gaming and social media platforms.</p>
<b>What are the best methods for promoting successful adherence to behavioural advice about COVID-19 whilst enabling mental wellbeing and minimising distress?</b>	<p>Understand how health messaging can optimise behaviour change, and reduce unintended mental health issues.</p> <p>Track perceptions of and responses to public health messages to allow iterative improvements, informed by mental health science.</p>	<p>Synthesise evidence base of lessons learned for future pandemics, tailored to groups as required.</p> <p>Motivate and enable people to prepare psychologically and plan practically for possible future scenarios.</p> <p>Understand the facilitators and barriers for activities that promote good mental health (such as exercise).</p> <p>Promote people's care and concern for others, fostering</p>

		collective solidarity and altruism.
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## **Panel 2: Populations of interest, including vulnerable groups**

**Whilst the whole population is affected by the COVID-19 pandemic different sections of the population will experience it differently** – for example:

- **Children, young people and families:** impacts of school closure particularly related to exposure to substance misuse, gambling, domestic violence and child maltreatment, lack of free school meals, accommodation and overcrowding, parental employment, change/disruption of social networks.
- **Older adults and those with multi-morbidities:** isolation, loneliness, end of life care and bereavement, the digital divide.
- **People with existing mental health issues, including those with SMI:** relapse, disruptions to services, isolation, pandemic-related information and behaviours exacerbating symptoms, changes in Mental Health Act.
- **Frontline healthcare workforce:** fears of contamination, moral injury, disruption of normal supportive structures, work stress, retention, enhanced confidence/skills.
- **Excluded groups:** e.g. prisoners, the homeless, refugees.
- **Society:** increased health inequalities, increased foodbank use, increased social cohesion/communitarianism, increased race-based attacks/trauma; rural communities.
- **People with learning difficulties:** change/disruption to support and routines, isolation, loneliness, risk of abuse.
- **People on low incomes:** job and financial insecurity, cramped housing, limited access to internet and technology.

## **4. Neuroscience: effects of the virus on brain health and mental health**

Almost nothing is yet known with certainty about the impact of SARS-CoV2 infection on the human nervous system. SARS-CoV2 is a zoonotic virus, and we know that about half of recent zoonotic epidemics have been caused by neurotropic viruses that can invade the central nervous system (CNS). The closely related coronaviruses responsible for the severe acute respiratory syndrome (SARS, 2002) and the Middle East respiratory syndrome (MERS, 2012) are biologically neurotropic and clinically neurotoxic, causing mental health and neurological disorders<sup>93–95</sup>. SARS-CoV2 is genetically almost identical to the SARS-CoV coronavirus, and likely to share its neurotropism and neurotoxicity.

Neurological symptoms of COVID-19 infection are common, diverse, and often severe. In a retrospective study of 214 patients in Wuhan, China, 36% had CNS symptoms or disorders and the subgroup of 88 patients with severe respiratory disease had significantly increased frequency of CNS problems (45%)<sup>96</sup>. The problems reported include dizziness, headache, loss of smell (anosmia), loss of taste (ageusia), muscle pain and weakness, impaired consciousness, and cerebrovascular complications. Similar reports have begun to emerge from Italy<sup>97</sup>. Some of these acute neurological presentations could reflect systemic aspects of infection, such as disseminated

intravascular coagulation causing strokes, or intense inflammation and hypoxia causing delirium.

SARS-CoV2 infection of the brain could be a major contributor to the core medical syndrome of respiratory distress and failure in COVID-19 patients<sup>98</sup>. Viral infection of the lung alveoli is the immediate cause of SARS; but viral infection of the brain stem nuclei could disrupt the normal rhythms and homeostatic control of respiration. This idea needs to be rapidly tested<sup>98</sup>: if brain stem infection does contribute to SARS-severity and ICU-dependency, that could be directly relevant to the immediate COVID-19 crisis in the NHS and other healthcare systems.

In the longer term, SARS-CoV2 could persistently replicate and proliferate in the brain with direct neurotoxic effects and immune-mediated neurotoxic effects. The Spanish flu epidemic of 1918-19 was linked to a spike in incidence of post-encephalitic Parkinsonism<sup>99</sup>. Currently, it is not known if SARS-CoV2 infection of the brain could cause mental health or neurodegenerative disorders, immediately or years after the acute respiratory phase of COVID-19 has passed; but immediate action is needed to build the research capacity to test these potentially important biological causes of COVID-19 related mental illness.

**Table 3. Neuroscience: effects of the virus on brain health and mental health**

<b>Immediate actions</b>	<b>Strategic research programmes</b>
Build a neuro-psychological database on UK COVID-19 cases (standardised, longitudinally repeated, data at scale; clinically and geographically inclusive)	<p>Understand how SARS-CoV2 might enter and propagate through the brain and how the immune response to SARS-CoV2 infection contributes to mental health and neurological symptoms</p> <p>Investigate the long-term relationship between SARS-CoV2 infection and post infective fatigue or depressive syndromes</p> <p>Validate clinical biomarkers of SARS-CoV2 brain infection using MRI and other methods</p>
Expand facilities for SARS-CoV2 tissue handling	Develop interventions to interrupt or prevent the adverse biological impacts of COVID-19 on brain function and mental health, including drug repurposing

### ***Immediate actions***

**A neuro-psychological database on COVID 19 cases needs to bring together standardised, longitudinally repeated, data at scale** both from the clinic for those



needing hospital treatment and by online assessments for patients in isolation at home. Following the progression of clinical symptoms over time will be key to understanding and predicting the effects of infection on the CNS.

**Facilities for SARS-CoV2 tissue handling need to be expanded** to examine human brain tissue post mortem, crucial to understanding the neurotropic and neurotoxic properties of the virus. Facilities equipped to safely handle human (or animal) brain tissue infected with SARS-CoV2 are currently very limited. We recommend building pathology and molecular neuroscience networks to enable brain and other tissue to be collected at autopsy and examined for viral infection and damage. This will require protocols for tissue collection and examination in appropriate laboratory facilities to protect researchers and other staff at all times.

### ***Longer term research priorities***

#### **Mechanisms by which SARS-CoV2 might enter the brain need to be understood.**

There are two likely pathways: neuronal and vascular<sup>100</sup>. The neuronal pathway used by other coronaviruses<sup>101,102</sup> is to invade a specialist sensory receptor in peripheral tissue, travel by axonal transport systems to the brain stem, and propagate between neurons by trans-synaptic mechanisms. We need to know if SARS-CoV2 can follow the same path to infect the human brain and whether it invades nerve cells by “hijacking” angiotension converting enzyme 2 (ACE2)<sup>103-105</sup>, despite neurons expressing low levels of ACE2<sup>106-108</sup>. SARS-CoV2 could invade the brain from the blood if circulating particles of the virus were transported across the blood-brain barrier by binding to ACE2 receptors expressed by endothelial cells<sup>108</sup>, or if infected leucocytes could carry the virus with them as they migrate into the tissues as part of the immune response to infection<sup>109</sup>. We also need to better understand how the intense systemic immune response to SARS-CoV2 infection impacts mental health and neurological symptoms<sup>96,110,111</sup> as well as the mechanisms of immune clearance of SARS-CoV2<sup>112,113</sup>.

Post infectious fatigue and depressive syndromes have been associated with epidemics, and it seems likely that the same will be true of the current pandemic. Longitudinal studies, especially if commenced before or soon after the start of the current pandemic, will be crucial in establishing the often complex biological pathways between infection and mental health outcomes<sup>114-116</sup>.

**Candidate biomarkers need to be evaluated** to measure SARS-CoV2 infection of the human brain and brain stem in living patients, including magnetic resonance imaging (MRI – e.g. T2 FLAIR to assess possible inflammation), cerebral blood flow imaging (to measure vascular and metabolic effects), and magnetic resonance spectroscopy to measure neurochemicals and metabolites. 7 Tesla MRI has sufficient spatial resolution to measure functional connectivity between subcortical structures that constitute networks for respiratory control and distress<sup>117</sup>. Other methods could include sampling CSF or positron emission tomography (PET) to measure brain inflammation; self-reporting or behavioural testing of smell, taste and other cranial or vagal sensory functions; electrophysiological methods to measure brain stem function; and computerised tests of cognitive and emotional processing.

Informed by greater understanding of SARS-CoV2 infection on the nervous system, as well as more accurate biomarkers of brain infection in COVID-19 patients, **interventions need to be developed to interrupt or prevent the adverse biological impacts of COVID-19 on brain function and mental health.** Potential drug targets include putative mechanisms for neuronal invasion, inter-neuronal propagation, and immune clearance by SARS-CoV2. Biological and clinical validation of these or other targets would enable experimental medicine studies or early clinical trials of repurposed drugs. For example, ACE2 inhibitors already licensed for treatment of hypertension, or the serine protease TMPRSS2<sup>118</sup>, which co-operates with ACE2 to facilitate viral entry into cells, and is blocked by a licensed drug for reflux oesophagitis, have already been advocated as repurposable drugs. There are many other potential candidates for drug repurposing<sup>119</sup>, which could be a faster route to effective treatment for CNS infection than development of entirely new drugs or vaccines. Partnerships between researchers in academia and industry will be vital.

## 5. Infrastructure and opportunities

Many of the immediate priorities are for **surveillance** of general and specific populations for health impacts, ranging from health behaviours, psychological symptoms, neuropsychiatric disorders and mortality including, but not limited to, suicide. The other immediate priority is to **assemble cohorts** to determine longer term outcomes and provide a resource for nesting intervention studies, as well as a resource of interventions to monitor their effectiveness. We recommend three main routes, which we describe in more detail below. For each of these routes, **there is a need to coordinate existing research infrastructure** through shared protocols, research measures and data assets, as well as to uphold the highest standards of scientific and ethical review. We urge the mental health science community to combine agility in initiating new or adapting existing research with collective scrutiny and collaboration.

First, administrative data assets principally derived from existing **electronic health records**, with systems in place to interrogate these for research purposes, provide a means of identifying health impacts at scale. Health Data Research UK is coordinating national efforts. Examples include the Clinical Practice Research Database<sup>120</sup> (CPRD) and similar primary care databases; the Clinical Record Interactive Search<sup>121</sup> (CRIS) and related systems for the interrogation of mental health records; and for general hospital settings, CogStack<sup>122</sup> which provides near real-time information from health records, for example to provide feedback on neurological consequences of severe COVID-19<sup>123</sup>. These systems should be linked between mental health, acute medical and community health service providers to identify patterns and trends both in clinical populations and in individuals with confirmed or suspected COVID-19.

Second, surveillance through **recruitment platforms and existing cohorts** has the benefit of embedding research on COVID-19 into studies where participants' mental or cognitive health has previously been ascertained. Existing cohorts or data platforms that can be rapidly deployed for COVID-19 research are likely to be particularly valuable. Examples include the NIHR National Bioresource, a platform which already includes clinical data on participants and DNA, and could be deployed for rapid characterization of mental health and neurological symptoms. UK Biobank has successfully conducted a

web-based mental health survey on 160,000 individuals, and the ongoing neuroimaging studies of 100,000 individuals provide an ideal opportunity to image the impact of SARS-Cov-2 infection on the brain/brainstem via a pre- to post-imaging comparison.

Third, **novel population based studies** on mental health and COVID-19 should be established, both using appropriate epidemiologically robust survey methodology for the whole population and specific groups of particular interest (e.g. children and young people, frontline staff in health and social care, and people who have survived severe COVID-19). Priority should be given to assembling representative populations using explicit sampling frames. Finally, many other disciplines will be establishing similar studies and it is vital that the ascertainment of mental health should be embedded wherever possible.

Whether using established or new cohorts, **priority should be given to methods which can ascertain COVID-19 status, symptoms and behaviours in as close to real time as possible** providing a dynamic picture of change in illness status, social circumstances and behaviours. Questions on COVID-19 and mental health symptoms and social stressors can readily be pushed out via smartphones. Passive data from smartphones can also give high temporal resolution to behaviours related to the pandemic. Cohorts should gain permissions for record linkage including serological status when mass testing becomes available, and consent for recruitment into nested sub-studies including randomised trials of interventions.

Patient and public involvement in research is a critical underpinning component to research. Given that the entire population has lived experience of the COVID-19 pandemic, researchers will need to be particularly mindful of consulting and collaborating with patient and public groups that reflect the diverse groups being studied in developing protocols, conducting research and interpreting results (Panel 3).

### **Panel 3: Principles of good research practice in COVID-19 research**

**Study design:** Researchers must continue to articulate the patient group or population and the research question under study. *A priori* research questions are crucial. Sample size, sources of bias and study design need to be carefully considered and appropriate to the research questions.

**Ethics:** Research on human participants should maintain high standards of ethical practice, including seeking research ethics committee approval<sup>124</sup>. Committees now have fast-track procedures to expedite study start up. Ethical considerations for conducting COVID-19 related research have been published<sup>125,126</sup>.

**Vulnerable groups:** Researchers should recognise the capacity of the pandemic to exacerbate health inequalities within populations, particularly affecting people with established mental health issues (including SMI) and physical disability, those with precarious or no employment or housing, or other forms of social inequality, such as digital poverty<sup>40</sup>.

**Involvement of patients, people with lived experience and the public:** Researchers should continue to engage and involve their ultimate consumers, patients,

people with lived experience, the public and **service providers**, in mutually setting research questions, testing the acceptability of protocols and questionnaires, and the interpretation of results. Researchers should ensure that they discuss their research findings with participants.

**Harmonised data and measures:** There is an obvious need for researchers to use and share, where possible, full study protocols and measures. This will facilitate comparisons between data and projects.

**Open science, reproducibility and data sharing:** The urgency of the research effort should be a strong driver for the principle of reproducible science. The ready availability of analysis code and data is critical to verifying findings and the rapid peer review of study protocols<sup>127</sup>, prior to data collection, minimises waste and ensures conclusions are empirically sound.

**Interdisciplinary working:** The challenge of COVID-19 pandemic requires imaginative collaborations between disciplines, including but not limited to psychology, psychiatry, neuroscience, virology, intensive care units, and respiratory medicine, among many others. Previous experience with epidemics has shown the “essential role that the humanities and social sciences play in information, reduction of fear and stigma, prevention, screening, treatment adherence, and control policies”<sup>128</sup>.

**Collaboration and coordination:** Where possible, research protocols should be deployed at scale harnessing existing research infrastructures including the Clinical Research Networks, Biomedical Research Centres, Mental Health Translational Research Collaboration, MQ Data Science group, charities, service user groups and professional bodies. To avoid waste and protect against participant fatigue, it is vital that there is national coordination across research groups. International collaboration and a global perspective will be beneficial.

## 6. Call for action

**Multidisciplinary mental health science research must be central to the international response to the current pandemic**, given the potential impacts on individual and population mental health and its potential impact on the brain function of some of those affected by COVID-19. There are important immediate insights to be gained, which could provide evidence-based guidance on responding to this pandemic, as well as how to promote mental health and wellbeing and safeguard the brain should future waves of infection re-emerge (see Panel 4).

The research priorities across the social, psychological and neuroscientific aspects of this pandemic should be coordinated at a national and international level. **We urge UK research funding agencies to work with researchers, people with lived experience and others to establish a high level co-ordination group to ensure that the mental health science research priorities are addressed swiftly, and that a firm base is established for long term studies.** We need rigorous, peer-reviewed, ethically-approved research co-developed with people with lived experience

that can be translated into effective interventions, rather than the current uncoordinated approach with a plethora of underpowered studies and surveys.

**The immediate priority is collecting high quality data** on the mental health and psychological impacts of the COVID-19 pandemic across the whole population and vulnerable groups, and on brain function, cognition and mental health for COVID-19 patients at all clinical stages of infection and illness. These datasets must be brought together **under a national data portal** for rapid access and use.

**There is an urgent need for the discovery, evaluation and refinement of mechanistically-driven interventions to address the psychological, social and neuroscientific aspects of this pandemic.** This includes bespoke psychological interventions to boost resilience and minimize mental health risks across society and in vulnerable groups, and experimental medicine studies to validate clinical biomarkers and repurpose new treatments for the potentially neurotoxic effects of the virus. There is an urgent need for research to address the impact of repeated pandemic related media consumption and to optimise health messaging around COVID-19. Rising to this challenge will require **integration across disciplines and sectors, including industry and health and social care.**

**New funding will be required to meet these priorities, but it can be efficiently leveraged by the UK's world-leading neuroscience and mental health research infrastructure.** The UK must connect with international funders and researchers to support a global response to the mental health and neurological challenges of this pandemic. These are challenging times, but there is a tremendous opportunity for mental health science to serve society and benefit medicine in the long term.

#### **Panel 4: Rapid learnings to apply to future infection waves or pandemics**

The outputs of immediate research could help inform responses to future infection waves of pandemics, for example by identifying:

- Mechanisms to support vulnerable groups under pandemic conditions – such as front line health and social care staff and those with pre-existing mental health issues, young people and older adults – including coping strategies and preventative interventions.
- Interventions that reduce mental health issues and boost resilience, including those that can be repurposed.
- Solutions to the impact of repeated media consumption about COVID-19 on the mental wellbeing of the nation to help individuals stay informed by authoritative sources while preventing over-exposure and mitigating the impact of viewing traumatic content.
- Methods for promoting more successful adherence to behavioural advice about COVID-19 while enabling mental wellbeing and minimising distress to inform medical treatment.

#### **Contributors**

EB, EAH, MH, RCOC, VHP, IT and SW contributed to the literature review, conceptualisation, design and interpretation of surveys, and writing and editing of the manuscript as part of the core advisory group. CC contributed to and coordinated the

writing and editing of the manuscript. KC analysed the qualitative data gathered via the stakeholder survey. LA, CB, HC, IE, TF, AJ, IM, SM, AKP, RS, RCS, CMW and LY contributed to the drafting and formulation of the manuscript as part of the expert advisory group. TK, KK and AS contributed the drafting and formulation of the manuscript as part of the expert advisory group and by including lived-experience expertise. All authors approved the final version for submission.

### **Declaration of interest**

CB reports grants and personal fees from Acadia pharmaceutical company and Lundbeck, personal fees from Roche, Otsuka, Biogen, Eli Lilly, Novo Nordisk, AARP and Exciva, and grants from Synexus, outside the submitted work.

EAH reports grants from The Lupina Foundation, The OAK Foundation, The Swedish Research Council, outside the submitted work. EAH reports her primary affiliation is Department of Psychology, Uppsala University, Sweden and is also a professor at Division of Psychology, Department for Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden. EAH reports serving on the board of trustees of the charity MQ: Transforming Mental Health (UK) as chair of the research committee. She receives no remuneration for these roles. EAH reports serving on the Editorial Advisory Board of The Lancet Psychiatry, and is an Associate Editor of Behavior Research and Therapy. She is the F1000 prime: Clinical Psychology and Psychopathology Section Head and is on the Editorial Board of following journals: Current Opinion in Psychology, Clinical Psychology in Europe, and Cognitive Behaviour Therapy. EAH receives book royalties from Oxford University Press (Imagery and Cognitive Therapy) and Guilford Press (Imagery-Based Cognitive Therapy for Bipolar Disorder and Mood Instability). She receives occasional fees from clinical workshops and conference keynotes. She receives occasional consultancy fees from SBU: Statens beredning för medicinsk och social utvärdering (Swedish agency for health technology assessment and assessment of social services), Sweden.

AKP has been financially supported by UK taxpayers, the UK's Economic and Social Research Council, the British Academy, the Diana Award, the John Fell Fund, the Leverhulme Trust, Barnardo's UK, and the Huo Family Foundation in the past five years. As part of science communication and policy outreach activities, he has served in an unpaid advisory capacity to the Organization for Economic Co-operation and Development, Facebook Inc., Google Inc., and the ParentZone.

IT is a Trustee of MQ, which is a mental health charity dedicated to raise funds to support research into mental health. She is also on the Council for the Medical Research Council of the United Kingdom.

MH reports grants from Innovative Medicines Initiative, outside the submitted work.

CC reports that Academy of Medical Science staff, including herself, and activity costs for this work were supported by a core grant the Academy of Medical Sciences receives annually from the Government Department for Business, Energy & Industrial Strategy for policy, communications and public engagement. She also reports that her husband is an employee of Otsuka Pharmaceutical Europe Limited and is a Trustee of The McPin Foundation.

All other authors declare no competing interests.

### **Funding source**

LA is the Mental Health Leadership Fellow for the Economic and Social Research Council.

EB is a National Institute for Health Research (NIHR) Senior Investigator. This paper represents independent research part-funded by the National Institute for Health Research (NIHR) Biomedical Research Centre at Cambridge University Hospital NHS Trust and the University of Cambridge. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.

CC indicated that Academy of Medical Science staff, including herself, and activity costs for this work were supported by a core grant the Academy of Medical Sciences receives annually from the Government Department for Business, Energy & Industrial Strategy (BEIS) for policy, communications and public engagement.

MH is funded by the National Institute of Health Research Biomedical Research Centre at the Maudsley and a National Institute of Health Research Senior Investigator Award. This paper represents independent research part-funded by the National Institute for Health Research (NIHR) Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care. NIHR were not involved in any aspect of the publication and had no role in the decision to submit.

AKP received funding from the Huo Family Foundation.

RS indicated that all research at Great Ormond Street Hospital NHS Foundation Trust and UCL Great Ormond Street Institute of Child Health is made possible by the NIHR Great Ormond Street Hospital Biomedical Research Centre. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.

LY is an NIHR Senior Investigator and her research programme is partly supported by NIHR Applied Research Collaboration (ARC)-West, NIHR Health Protection Research Unit (HPRU) for Behavioural Science and Evaluation, and the NIHR Southampton Biomedical Research Centre (BRC).

The funding for TK's salary came solely from his employer, The McPin Foundation.

The views expressed are the views of the authors alone and do not necessarily represent the views of their organisations or funding sources.

## **Acknowledgements**

We are grateful to all staff at the Academy of Medical Sciences and MQ for their work in coordinating and supporting this project's secretariat and communications. Special thanks to Rachel Quinn, Nick Hillier, Helen Munn, Neil Balmer, Angeliki Yiangou, Fern Brookes, Holly Rogers, Claire Bithell, Naomi Clarke, Melanie Etherton, Tom Livermore, Dylan Williams and Daisy Armitage. We also extend our sincere thanks to Katie White, Carolin Oetzmann, Valeria de Angel and Dr Sumithra Velupillai at King's College London for their tremendous efforts in data analysis, and Dr Beau Gamble at Uppsala University and Dr Seonaid Cleare at University of Glasgow for their support with referencing. We are also grateful to the team at Ipsos MORI for their work on the online omnibus. Special thanks also to everyone who participated in the MQ and Ipsos MORI surveys for sharing their views and personal experiences during challenging times – we are hugely grateful to them for their openness and honesty about mental health and wellbeing. We are grateful to Professor Peter Jones for comments on an earlier draft.

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